THE REMARKS

Claims 1-11 and 17-21 were pending prior to entering the amendments.

The Amendment

Support for the amendments in the claims is listed as follows:

Claim 1:

"which can penetrate the plasma membrane" – page 5, 2nd paragraph, line 6;
"a signaling module which comprises an image creating compound selected from the group consisting of" – page 5, 1st paragraph, lines 4 to 6, and original Claim 6;
"the nuclear localization sequence is covalently coupled to the signalling module via a non-cleavable spacer" – page 7, 3rd paragraph.

Claim 3

The recited homeobox proteins are supported on page 5, 2nd paragraph, lines 19-21.

Claims 5 and 31

The recited nuclear localization sequences are supported on page 6, 4th paragraph.

Claims 22-24 and 30

A chelate complex and the recited examples are supported on page 7, 1st paragraph.

Claims 25, 26 and 29

The subject matter of a chemotherapeutical drug coupled to the conjugate is supported on page 16th, 2nd paragraph.

Claim 27

The structure recited in claim 27 is supported on page 8, 5th paragraph.

Claim 28

Claim 28 has the same support as those listed for claim 1 and claim 3.

No new matter is added in any of the amendments. The Examiner is requested to enter the amendment and re-consider the application.

The Response

Double Patenting Rejections

Claims 1, 2, 5-10, and 17-21 are rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-16 of U.S. Patent No. 7,531,502.

Claims 1, 5, 6, 10, 11, and 17-21 are rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-4 and 6 of U.S. Patent No. 7,563,761.

Claims 1, 5-8, 10, 11, and 17-21 are rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-10, 19, and 20 of U.S. Patent No. 6,821,948.

Applicant is submitting herewith a Terminal Disclaimer to obviate the above double-patenting rejections.

Provisional Double Patenting Rejection

Claims 1, 2, 5, 6, 9, 10, and 17-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-3, 6-8, 11, 13-16, 19, and 21 of copending Application No. 12/634,972.

Applicant wishes to defer this provisional rejection until the claims of this application are otherwise allowable.

35 U.S.C. § 112, First Paragraph Rejection – Written Description

Claims 1-11 and 17-21 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement.

Applicant has amended the claims such that Claim 1 meets the written description

requirement.

In particular the structure of the conjugate has been defined that the conjugate has the structure of:

transmembrane module – cleavable spacer - nuclear localization sequence – non-cleavable spacer – signaling module.

"Amphiphilic transport proteins of human origins" have been further characterized in that they can penetrate the plasma membrane. Such peptides are well recognized in the art as cell penetrating peptides (CPPs) and are widely used to deliver different types of cargo molecules across the plasma membrane. In the specification on page 5, 2nd paragraph penetratin and transportan are given as examples. The reference of Derossi et al. mentioned in connection with penetratin describes the mechanism of cell penetration by such peptides and recites further examples of cell penetrating peptides. Thus, the correlation between the amphiphilic nature and the cell penetrating function of such peptides was established in the art at the filing date of the application. Because cell penetrating peptides were well known in the art, one of ordinary skill in the art can immediately envisage what class of compounds are comprised by amphiphilic transport peptides of human origin which can penetrate the cell membrane. According to the MPEP "information which is well known in the art need not be described in detail in the specification (e.g. Hybritech, Inc v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986))". The passage on page 5, 2nd paragraph in connection with the method of Example 1 adequately guides one of ordinary skill in the art to identify further amphiphilic transport peptides of human origin according to the present invention. Therefore, it is described with sufficient particularity what amphiphilic transport peptides of human origin are compatible with the invention considering that the class of cell penetrating peptides was well known at the filing date of the application.

"Nuclear localization sequences (NLS)" have a clear meaning in the art; as defined in the attached article (Efthymiadis et al, J. Biol. Chem., 273:1623-1628, 1998): To enter the eukaryotic cell nucleus, proteins larger than 45 kDa require targeting signals called nuclear localization sequences (NLSs) defined as the sequences sufficient and necessary for nuclear localization of their respective proteins. Further, ten representative examples of NLS are recited on page 6, 4th paragraph. Thus, one of ordinary skill in the art can immediately envisage what nuclear localization sequence is compatible with the instant invention, because this class of peptides is

well known in the art and applicant has provided a sufficient description of a representative number of suitable species.

The claims have been amended to further define "Signaling module" by comprising an image creating compound selected from the group consisting of Gd, Ga, Mn, I, Fe, and F. Therefore, the "signaling module" has been limited to the species given on page 7, 1st paragraph of the specification.

The objected human homeobox protein HOX-B1 derivatives have been deleted from claim 3.

Claims 17-21 have been cancelled.

Thus, the terms of the claims as amended have been limited to subject matter which is described in the specification with sufficient particularity. Therefore, one of ordinary skill in the art can clearly envisage what combinations of the components are compatible with the claims. Hence, the claims as amended now satisfy the written description requirement.

35 U.S.C. § 112, Second Paragraph Rejections

Claims 1-11 and 17-21 are rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6, 10, and 17-21 are cancelled.

As discussed above, the amended Claim 1 is now clear and definite.

Claims 17-21 are rejected under 35 U.S.C. 112, second paragraph, as allegedly being incomplete for omitting essential steps, such omission amounting to a gap between the steps.

Claims 17-21 have been cancelled.

35 U.S.C. § 101 Rejection

Claims 17-21 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in a claim which is not a proper process claim.

Claims 17-21 have been cancelled.

Conclusion

Applicants believe that the application is now in good and proper condition for allowance. Early notification of allowance is earnestly solicited.

Respectfully submitted,

Date: July 26, 2010

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